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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/633,402	KLIMBERG ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,10-14,44-52,55 and 56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,10-14,44-52,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 6, 10-14, 44-53, and 55-56 are presented for examination

Applicants' amendment filed 12/3/2007 has been received and entered into the application. No claims are amended, cancelled, or added.

Applicants' arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statements filed on 12/3/2007 and 1/3/2008. The Examiner has considered the references cited therein to the extent that each is a proper citation. USP No. 3,085,942 as cited in the IDS filed 1/3/2008 was not considered because it appears to be an incorrect citation. For example, the patentee, publication date, and filing date do not correspond to USP No. 3,085,942. As such it is not clear if the patent number is correctly cited. Please refer to the attached USPTO Form 1449.

Response to Arguments

Applicant's arguments filed 12/3/2007 have been fully considered but they are not persuasive. In traversing the rejections set forth in the Non-Final Office Action mailed 6/1/2007, Applicants present the following arguments.

Firstly, with respect to the 35 U.S.C. 103 rejection of claims 6, 10-14, 44-52, and 55-56 as being unpatentable over Willmore et al. in view of Shinal et al. and Good et al., Applicants argue that the individual references do not teach or suggest the limitations of the instant claims. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, while the individual references taken alone may not teach or suggest the limitations of the instant claims, it is the combination of the cited references that renders prima facie obvious the claimed methods. As an example, Applicants argue that Willmore et al. do not teach oral administration as instantly claimed. However, it is noted that Shinal et al. teach and suggest that glutamine and a carbohydrate can be administered in combination. See Shinal et al. at page 31, line 25 to page 32, line 9 wherein powdered drink mixes reconstituted with water, juice, or other liquids are taught that imply oral administration as instantly claimed. Further, Willmore et al. teach compositions comprising glutamine so as to protect tissue against oxidative injury, including radiation-associated oxidative damage, thus motivating the administration of glutamine to patients undergoing radiation therapy. Shinal et al., when taken in combination with Willmore et al., provides the motivation to add a carbohydrate to the glutamine compositions of Willmore et al. wherein they teach that carbohydrates increase the cellular uptake of bioactive agents, including glutamine as instantly claimed (Abstract; page 6, lines 1-11). As such, one of ordinary skill in the art at the time of the invention would have been motivated to add a carbohydrate to the glutamine compositions of Willmore et al. and to subsequently administer the resulting

composition to a patient undergoing radiation therapy. Accordingly, in view of the teachings of the combined references, the instantly claimed methods of protecting tissue against damage from radiation would have been prima facie obvious at the time the invention was made. The rejection is maintained for the reasons of record and reiterated below.

Secondly, with respect to the Obvious-Type Double Patenting rejection of claims 6, 10-14, 44-52, and 55-56 over claim 1 of USP No. 7,186,517 in view of Shinal et al. and Good et al., Applicants state that upon notification of otherwise allowable subject matter, they will file a terminal disclaimer to overcome this rejection. As no pending claims can be indicated as allowable until the filing of a terminal disclaimer, the rejection is maintained for the reasons of record and reiterated below.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 6, 10-14, 44-53 and 55-56 are again rejected under 35 U.S.C. § 103(a) as being unpatentable over **Willmore *et al.*** (U.S. Patent No. 5,248,697) in view of **Shinal *et al.*** (WO 00/69470; Published Nov. 23, 2000) in view of **Good *et al.*** (U.S. Patent No. 6,666,811) (previously cited).

The instant claims recite methods of protecting tissue against damage from radiation therapy comprising orally administering an aqueous composition comprising glutamine and about 20-40 wt-% carbohydrate.

Willmore summarizes its disclosure in the abstract wherein glutamine is described as protective against oxidative injury to tissue as a result of treatment and specifically cites radiation-associated oxidative damage in the last three lines therein. Thus, Willmore is directed to glutamine administration for its protective effects against radiation as instantly claimed in claims 10-14. Willmore also indicates the radiation therapy therein discussed is directed to cancer patients as cited in column 2, lines 46-57, and more particularly, breast cancer patients as described in column 7, line 66, through column 8, line 9, as instantly claimed. Glutamine administration in dosages within the ranges of instant claims 44-47 are cited in Willmore in column 6, lines 22-34, as well as orally administered as instantly claimed in column 6, lines 22-48. Willmore does not teach the co-administration of carbohydrate to radiation therapy nor the higher dosage of radiation that may be utilized thereby as instantly claimed.

However, Shinal *et al.* describe compositions and methods for increasing the cellular uptake of bioactive agents, including glutamine as instantly claimed (Abstract; page 6, lines 1-11), thus motivating the combination of glutamine and a carbohydrate as instantly claimed. The invention describes such compositions and methods as solutions or dispersions comprising an

aqueous vehicle and an effective amount of a bioactive compounds in combination with an amount of carbohydrate effective to reduce absolute solubility of the bioactive agent in the aqueous vehicle so as to achieve increased absorption of the bioactive agent into target cells (page 3, lines 4-11). The compositions and methods described therein are taught to increase the gastrointestinal epithelial cell uptake of the amino acid glutamine by a factor of over 150x (page 5, lines 19-23). With respect to oral administration as recited in the instant claims, Shinal et al. at page 31, line 25 to page 32, line 9 teach powdered drink mixes reconstituted with water, juice, or other liquids which implies oral administration as instantly claimed. Carbohydrates include monosaccharides, disaccharides and sugar alcohols as recited in instant claims 48-49 (page 3, lines 20-29). The ratio of carbohydrate to active agent is taught to be in the range of 1.5:1 to 20:1, preferably 4:1 to 15:1 in the final aqueous solution thus meeting the limitations of claims 50-51. The limitation "about 20-40 wt-% carbohydrate" as recited in claim 6 is taught at page 10, lines 6-33 wherein 20% to 99%, 15-50%, 30-50% and 20-40% carbohydrate carriers are disclosed. A composition comprising no naturally occurring amino acids other than glutamine is disclosed (*id.* at lines 29-33).

Good *et al.* at column 54, lines 23-35, suggests that radiation therapy to be effective requires a dose much higher than that applied to normal tissue and thus motivates utilizing high radiation dosages which reasonably are made more feasible via any protective effect of normal tissue to radiation as provided by the glutamine administration of Willmore. This also provides a reasonable expectation of success for utilizing increased radiation therapy. Motivation to do so is supplied in Good and the added protective effects of glutamine administration are described in

Willmore. Breast cancer therapy, as instantly claimed, is recognized in Good as being a radiation treatable cancer in column 59, lines 28-33, as also instantly claimed.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the instant invention to utilize high radiation dosages permitted by glutamine protection, as taught in Willmore and motivated by Good, combined with the glutamine absorption enhancing effect of a carbohydrate as suggested and motivated by Shinal *et al*. The skilled artisan would have been imbued with at least a reasonable expectation that orally administering a composition comprising glutamine and a carbohydrate would be protective of tissue against radiation therapy as taught by Willmore *et al*.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6, 10-14, 44-52 and 55-56 are again rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 7,186,517 in view of Shinal *et al.* (WO 00/69470) and Good *et al.* (U.S. Patent No. 6,666,811). In the instant case, the monitoring methodology as claimed in the '517 patent comprises administration of glutamine to a human breast cancer patient undergoing radiation therapy. The administration methodology of the '517 patent is explained via utilizing its specification as a Dictionary for such administration wherein column 3, lines 19-20 defines administration to include oral administration as instantly claimed. The '517 patent is also used via its specification, in Example 2 at columns 5-6, as a Dictionary regarding defining the amount of glutamine administration to be within the instantly claimed ranges of instant claims 44-47.

Shinal *et al.* has been previously cited for teaching the administration of carbohydrate so as to increase the absorption of glutamine. Carbohydrates are administered in the ratios as instantly claimed.

Good *et al.* at column 54, lines 23-35, suggests that radiation therapy to be effective requires a dose much higher than that applied to normal tissue and thus motivates utilizing high radiation dosages which reasonably are made more feasible via any protective effect of normal tissue to radiation as provided by the glutamine administration of the '517 patent. Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to

utilize high radiation dosages that are permitted by glutamine protection, as monitored also in the '517 patent and motivated by Good. The additive effect of a carbohydrate is beneficial when administering glutamine to a patient according to Shinal *et al.* and results in the practice of the instantly claimed invention.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614